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Diagnostic importance of mean platelet volume, platelet distribution width and platelet large cell ratio as screening tool in immune thrombocytopenia

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Abstract

Objective: To determine diagnostic importance of mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR) in diagnosing cases of immune thrombocytopenia.

Methodology: The study was done in Khyber Teaching hospital from January 2017 to May 2018. Cases with low platelet count of all the ages and both the genders were included in the study by non probability purposive sampling technique and were subjected to bone marrow aspiration to rule out other causes of thrombocytopenia and thus confirm the diagnosis of immune thrombocytopenia. The platelet indices were noted and their sensitivity, specificity and accuracy were determined for immune thrombocytopenia. Mean and standard deviation were used for quantitative data. Percentage and frequency were used to measure qualitative data. Data was analysed by SPSS.

Results: 84 cases with thrombocytopenia of mean age 23.4 ± 12.1 years (range 7–81 years) were included in the study. There were 38 (45.2%) males and 46 (54.8%) females. There were 40 cases of immune thrombocytopenia. The sensitivity and specificity for PDW (59.1% and 43.1%, respectively), MPV (59.1% and 52.9%, respectively), and PLCR (50% and 52.9%, respectively) were found low to be used as screening tool for immune thrombocytopenia.

Conclusion: The MPV, PDW and PLCR has low sensitivity and specificity and therefore should not be used as reliable screening tool in giving preliminary diagnosis of the immune thrombocytopenia.

Keywords: immune thrombocytopenia, mean platelet volume, platelet distribution width

Introduction

Immune thrombocytopenia is a common auto immune disease in which platelet count is reduced in blood leading to petechiae and hemorrhage.[1] The incidence of immune thrombocytopenia is about 6 per 100,000 individuals annually in the United States.[2] Similar incidence is reported from United Kingdom.[2] The incidence in Europe is about 2.68 per 100,000 population.[3] In immune thrombocytopenia, the platelet count is decreased because there are autoantibodies in circulation against platelets that bind to platelets surface and destroy them in the spleen.[1,2] In most cases, it results from preceding viral infections of upper respiratory tract. The disease usually presents as mild petechiae on mucosal surfaces, but may present as serious gastro intestinal bleeding or epistaxis.[1]

Bone marrow aspiration is done to exclude causes of thrombocytopenia other than immune thrombocytopenia.[1,4] Although, anti platelet antibodies are also detected in this disease but these are not specific test for immune thrombocytopenia.[2] This is so because in some cases of immune thrombocytopenia, these antibodies are not detected while the same antibodies may be found in diseases other than immune thrombocytopenia.[2] With advanced technology, the hematology analyzers can now give us certain parameters that can give information about platelets.[2] These parameters are referred to as platelet indices in literature.[2,5]

Platelet indices include mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR).[2,6] The proposed normal value of MPV is 7.2 to 11.7 fL.[6] in immune thrombocytopenia, when the platelets gets destroyed in the spleen, the new platelets that are being formed in the bone marrow are larger ones than the normal and thus the MPV increases in immune thrombocytopenia.[6] The value of PDW ranges from 8.3% to 56.6% in healthy individual.[6] It is the measure of variability in size of platelets.[6] The changes in the PDW and MPV are always in the same direction, that is, if MPV increases, PDW also increases and vice versa.[6] PLCR tells about the percentage of the larger platelets in circulation.[6] Normal

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PLCR in healthy individual ranges from 15% to 35%.[6] The values of these indices are same in males and females.[7]

A *screening test* is a test that is applied to individuals in order to detect the presence or absence of a disease in them.[8] The people who give positive result with a screening test are further subjected to a confirmatory test and thus the final diagnosis is made.[8] The confirmatory test is sometimes called the gold standard test. Ideally, a screening test should give a positive result only if the person actually has the disease and vice versa.[8] The screening test is done first because the confirmatory diagnostic gold standard test may be expensive, or invasive, or the result may take time.[8]

Screening test is assessed in terms of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).[8]*Sensitivity* is defined as the ability of the test to detect a disease in a person who actually has the disease.[8]*Specificity, on the other hand,* is the ability of a test to identify the person as negative, who actually does not have a disease.[8] A screening test is considered good one if it has high sensitivity and high specifcity.[8] PPV is the probability of a person who has the disease to give a positive result with a test, while NPV is measure of the probability that a person who does not have a disease will give negative result with the test.[8]

The diagnostic importance of a screening test is measured by determining area under the reactive operative characteristic (ROC) curve.[9] A good test has a larger are under the curve (AUC) and vice versa A weak test has AUC of about .5 to .6 .A good test has the AUC of about .75 to .9. An excellent test has AUC of .97 to 1.[9]

It is well known that the red cell indices like mean cell volume and red cell distribution width are used to investigate anemias.[10] However when it comes to platelet indices, the researchers are unclear about the role of platelet indices in thrombocytopenia.[10] Currently, most of the studies are done only on importance of platelet indices in differentiating hypoproductive versus hyper-destructive thrombocytopenias.[4,5,9] So, we conducted this study with an intend to determine the diagnostic significance of platelet indices as screening tool for immune thrombocytopenia.

Methodology

This Cross sectional analytical study was conducted in Khyber Teaching Hospital, Peshawar from January 2017 to May 2019, that is, 17 months duration. Ethical approval was obtained from the Ethical Committee of the Institution after ensuring that patients data is anonymised and that there will be strict privacy of the patients demographics. About 84 cases referred to the hematology section for work up of thrombocytopenia were included in the study. Cases whose platelet indices were not present in the complete blood count (CBC) slip and where diagnosis could not be made on the bone marrow aspirate biopsy were excluded from the study.

About 2 mL venous blood sample was taken from each patient by a trained phlebotomist. The blood was immediately transferred to EDTA tube. The tube was gently moved so that proper mixing of blood with anticoagulant is ensured. Bone marrow aspiration was done and aspirate smears were prepared and stained using Giemsa stain. The blood sample was handed over to the laboratory technician to be run in hematology analyser (Sysmex XP-300). The blood counts, blood smears and bone marrow aspirate smears were examined by expert hematologists. The platelet indices were analysed whether they could determine immune thrombocytopenia or not. Other causes of thrombocytopenia were excluded before making diagnosis of immune thrombocytopenia.

Data was analysed by SPSS. Mean and standard deviation were used for quantitative variables. Frequency and percentages were used to measure qualitative data. Sensitivity, specificity, area under curve (AUC), negative predictive value, positive predictive value and likelihood ratios were determined for each of the PDW, MPV, and PLCR. Cut off values were taken from ROC curve by using Youdens index formula (sensitivity – specificity) – 1. The accuracy and likelihood ratios were calculated as per following formulae

$$\text{Accuracy} = \frac{\text{True positive} + \text{True negative}}{\text{True positive} + \text{True negative} + \text{False positive} + \text{False negative}}$$

$$\text{Likelihood ratio for positivetest} = \frac{\text{True positive}/(\text{True positive} + \text{Fasle negative})}{\text{False positive}/(\text{False positive} + \text{True negative})}$$

$$\text{Likelihood ratio for negativetest} = \frac{\text{False negative}/(\text{True positive} + \text{False negative})}{\text{True negative}/(\text{False positive} + \text{True negative})}$$

Results

Out of 84 cases of thrombocytopenia, about 40 cases were of immune thrombocytopenia mean age of the study sample was 23.4 ± 12.1 years (range 7–81 years). There were 38 (45.2%) males and 46 (54.8%) females. The sensitivity and specificity of PDW, MPV and PLCR for different cut off values are shown in Table 1. Receiver operative characteristic (ROC) curve for each

Table 1

Sensitivity, specificity, positive predictive value, negative predictive value, accuracy and likelihood ratios for PDW, MPV and PLCR in cases of immune thrombocytopenia

Platelet indices	Cut off values	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)	Likelihood ratio	
							Positive Likelihood ratio (LR+)	Negative likelihood ratio (LR−)
PDW (%)	>12.95	61.4	43.1	51.9	60.0	55.3	1.2	.75
	>13.20	59.1	51.0	58.5	62.3	60.6	1.5	.75
MPV (fL)	>9.35	59.1	52.9	37.3	28.0	39.2	.68	2.8
	>9.45	50.0	58.8	33.3	29.4	31.9	.56	2.7
PLCR (%)	>21.9	61.4	33.3	39.7	34.6	38.2	.74	2.1
	>24.05	50.0	52.9	38.6	40.5	39.3	.71	1.6

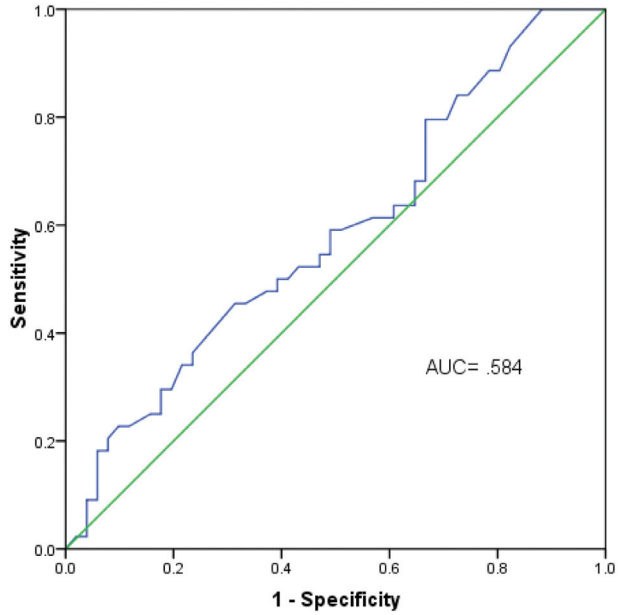

Figure 1. ROC curve for PDW at 95% confidence interval (AUC = .584).

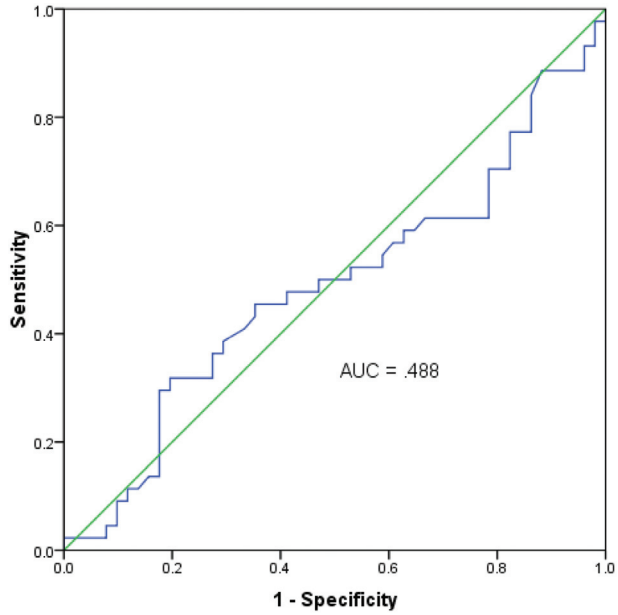

Figure 3. ROC curve for PLCR at 95% confidence interval (AUC = .488).

of the PDW, MPV and PLCR are shown in Figures 1, 2 and 3, respectively.

Discussion

There are a number of causes of thrombocytopenia and an important common cause that clinicians frequently see is immune thrombocytopenia.[10] The antibodies against platelet surface receptors are produced in the body because of certain viral infections of the respiratory tract and also certain drugs and vaccinations.[1]

The red cell indices like mean cell volume and red cell distribution width are confidently used to assess anemias.[10]

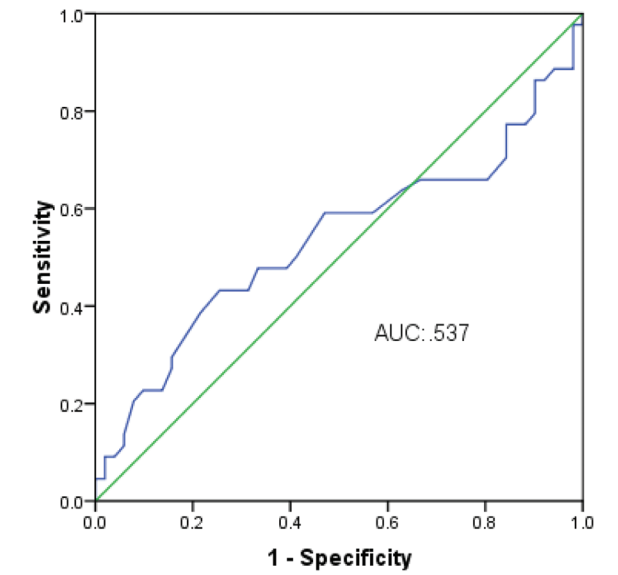

Figure 2. ROC curve for MPV at 95% confidence interval (AUC = .537).

However, when it comes to platelet indices, it is still debatable whether these indices have any diagnostic utility in cases of thrombocytopaenia.[10] No doubt, the platelet indices can differentiate hypoproductive thrombocytopenias from the hyper-destructive ones, yet there use as a screening tool in different causes of thrombocytopenia needs more work.[11]

We find in our study that the platelet indices namely MPV, PDW and PLCR have low sensitivity and specificity in screening immune thrombocytopenia patients. In a study done by Chandra in 2010, the sensitivity and specificity of MPV at a cut-off point of 8.15 fL was only 67.7% and 65%, respectively.[12] Chandra suggested that bone marrow biopsy should be preferred rather than relying on MPV as screening test.[12] In another study done by Tang in 2017, PDW was suggested as a poor screening tool for diagnosing immune thrombocytopenia.[1] In the same study, MPV had sensitivity and specificity of 70.3% and 74.8%, respectively, a figure not good enough to recommend MPV as a good screening tool for immune thrombocytopenia.[1] Ntaios reported that PDW and MPV had high diagnostic significance but PLCR had low value.[13] Norrasethada in 2019 proposed the sensitivity and specificity of 77% and 89%, respectively for MPV.[14] However, study done by Aponte-Barrios in 2014 reported a high sensitivity and specificity for MPV, PDW and PLCR in diagnosis of immune thrombocytopenia and stresses on the use of these indices as screening tool.[9] Al-Sharifi proposed a cut off value of 9.9 fL for MPV with sensitivity and specificity of 100%.[15] Our study differ from above mentioned studies in that the platelet indices had poor sensitivity and specificity for diagnosing immune thrombocytopenia.

It is a common observation in cases of thrombocytopenia that if platelet count is very low, the hematology analyser does not give the reading of platelet indices on the CBC slip.[11] So the information from the platelet indices can not be availed in those cases. Also, on the basis of the finding in our study that these indices have a low sensitivity and specificity in diagnosing immune thrombocytopenia, the clinicians must not rely upon these indices solely and bone marrow aspiration should be preferred while suspecting immune thrombocytopenia.

Conclusions

The MPV, PDW and PLCR should not be relied upon as screening test for immune thrombocytopenia.

Limitations

This study was conducted in a single tertiary care center and hence the figures generated may not represent the whole population.

Recommendations

We recommend that more research should be done to devise new platelet parameters that can be helpful as screening tool in immune thrombocytopenia. also we recommend the use of bone marrow as diagnostic test for immune thrombocytopenia rather than relying on platelet indices solely.

Conflicts of interest

The authors declare no conflicts of interest.

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